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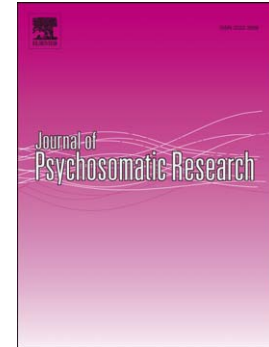
Exploring an association between hostility and serum concentrations of TNF- α and its soluble receptors

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Exploring an association between hostility and serum concentrations of TNF- α and its soluble receptors

(Short title: Hostility, TNF- α and sTNF-R levels)

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Letter to the Editors

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Cytokines, tumor necrosis factor (TNF)-alpha, soluble TNF receptors, hostility

Dear Editors,

With great interest and pleasure, we have read the article “The relation between hostility and concurrent levels of inflammation is sex, age, and measure dependent” by Boisclair Demarble et al. [1] in the Journal of Psychosomatic Research which reports an association between hostility and TNF- α serum levels in women, but not men. It also gives a comprehensive overview of the somewhat contradictory results regarding cytokine levels and hostility reported in the literature. As several of the cited studies measured TNF- α levels [e.g. 2, 3], we thought that it would be of value to investigate hostility and levels of TNF- α , as well as its soluble receptors p55 (sTNF-R p55) and p75 (sTNF-R p75), in a cross-sectional study examining 135 male German soldiers [4].

In this study [4], the participating soldiers were assessed using the Brief Symptom Inventory (BSI) [5], which is an instrument that evaluates psychological distress and symptoms of psychiatric disorders. It is a 53-item self-report scale that takes approximately 10 minutes to complete. It contains subscales that address the following areas: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobia, paranoia and psychoticism.

Blood was also drawn from study participants. Blood probes were immediately centrifuged at 3000 rpm for 10 min. The supernatant was aliquoted and stored in non-absorbing polypropylene tubes of 300 μ l. Probes were shock-frozen in liquid nitrogen and stored in freezers at -80 °C until further measurement. TNF- α and its soluble receptors sTNF-R p55 and p75 were measured using a Bio-Plex Pro™ human cytokine immunoassay from Bio Rad, Germany.

In the Pearson correlation analysis, serum levels of TNF- α and its soluble receptor sTNF-R p75 were not significantly correlated with any of the BSI subscales. This is consistent with the finding that there is no association between hostility and TNF- α serum levels in men, as reported by Boisclair Demarble et al. [1]. However, sTNF-R p55 levels correlated significantly ($p < 0.05$) with all BSI subscales: somatization ($r = 0.203$, $p = 0.021$, $N = 129$), obsessive-compulsive ($r = 0.233$, $p = 0.008$, $N = 129$), interpersonal sensitivity ($r = 0.263$, $p = 0.003$, $N = 129$), depression ($r = 0.187$, $p = 0.033$, $N = 129$), anxiety ($r = 0.230$, $p = 0.009$, $N = 129$), hostility ($r = 0.249$, $p = 0.004$, $N = 129$), phobia ($r = 0.185$, $p = 0.036$, $N = 129$), paranoia ($r = 0.285$, $p = 0.001$, $N = 129$), and psychoticism ($r = 0.206$, $p = 0.019$, $N = 129$). We also reported [4] that body mass index (BMI) had a significant effect ($F[1, 100] = 7.36$; $p = 0.008$) on sTNF-R p55

levels, but also on TNF- α and sTNF-R p75 levels in this sample. In a regression analysis, hostility contributed significantly to sTNF-R p55 levels ($F(1, 127)=8.41$; $p=0.004$; corrected $R^2=0.055$) even when controlling for BMI.

Our results support the view of Boisclair Demarble et al. [1] that hostility and TNF- α serum levels are not related in men. In addition to the importance of sex and age highlighted by Boisclair Demarble et al. [1], we would like to emphasize the influence of BMI on the TNF- α system. Based on our data, with regards to TNF- α signaling, we recommend that TNF- α receptors should also be taken into account. To our knowledge, this is the first report on correlations between sTNF-R p55 levels and hostility.

As sTNF-R p55 levels are related to several BSI subscales, one may consider psychological associations between these subscales. For example, hostility could be a consequence of paranoid thoughts. The answers to these questions, however, are beyond the scope of our data. Elevated TNF-R p55 levels have also been identified in other conditions like depression [6, 7], therefore, suggesting they may be a general indicator of psychological problems, rather than a specific marker for hostility.

Conflict of interest

The authors state that they do not have any conflicts of interest with regards to this article.

Acknowledgement

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References

- 1) J. Boisclair Demarble, D.S. Moskowitz, J.C. Tardif, B. D'Antono, The relation between hostility and concurrent levels of inflammation is sex, age, and measure dependent, J. Psychosom. Res. 76 (2014) 384-393.
- 2) E.C. Suarez, J.G. Lewis, C. Kuhn, The relation of aggression, hostility, and anger to

lipopolysaccharide-stimulated tumor necrosis factor (TNF)-alpha by blood monocytes from normal men, *Brain Behav. Immun.* 16 (2002) 675–684.

- 3) D. Janicki-Deverts, S. Cohen, W.J. Doyle, Cynical hostility and stimulated Th1 and Th2 cytokine production, *Brain Behav. Immun.* 24 (2010) 58–63.
- 4) H. Himmerich, G.D. Willmund, P. Zimmermann, J.E. Wolf, A.H. Bühler, L.M. Holdt, D. Teupser, K.C. Kirkby, U. Wesemann, Serum concentrations of TNF- α , sTNF-R p55 and p75 and post-traumatic stress in German soldiers, *Eur. Cytokine Netw.* 26 (2015) 57-60.
- 5) L.R. Derogatis, N. Melisaratos, The Brief Symptom Inventory: an introductory report, *Psychol. Med.* 13 (1983) 595-605.
- 6) H. Himmerich, S. Fulda, J. Linseisen, H. Seiler, G. Wolfram, S. Himmerich, K. Gedrich, S. Kloiber, S. Lucae, M. Ising, M. Uhr, F. Holsboer, T. Pollmächer, Depression, comorbidities and the TNF-alpha system, *Eur. Psychiatry* 23 (2008) 421-429.
- 7) R. Grassi-Oliveira, E. Brietzke, J.C. Pezzi, R.P. Lopes, A.L. Teixeira, M.E. Bauer, Increased soluble tumor necrosis factor-alpha receptors in patients with major depressive disorder, *Psychiatry Clin. Neurosci.* 63 (2009) 202-208.